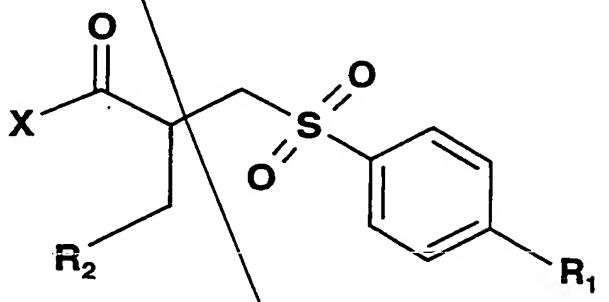
CLAIMS

1. A compound which is a 3-arylsulfonyl-2-methyl propanoic acid derivative of formula (I):



(I)

wherein

X is HO-NH- or HO-;

R_1 is selected from phenyl, 4-chlorophenyl, 4-fluorophenyl, 4-cyanophenyl, benzamido (i.e., -NH-CO-Ph) and benzamido substituted on the terminal phenyl ring by C_1-C_4 alkyl, fluoro, chloro, cyano or C_1-C_4 alkoxy;

R_2 is selected from:

(a) –S-Ar or –S-CH_2-Ar, wherein Ar is a monocarbocyclic or bicarbocyclic aromatic moiety which is either unsubstituted or substituted with one or two substituents selected from C_1-C_4 alkyl, phenyl, benzyl, C_1-C_4 alkoxy, fluoro, chloro, bromo, nitro, cyano, hydroxy, amino, dimethylamino, acetamido, methylthio and acetyl;

(b) –O-Ar, wherein Ar is as defined above;

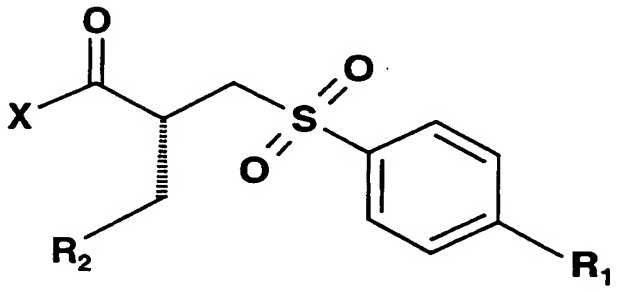
(c) -S-Het or –S-CH_2-Het, wherein Het is a heterocyclic ring selected from pyridine, pyrimidine, pyridazine, pyrazine, 1,2,5-triazine, imidazole, thiophene, furan, pyrrole, pyrazole, 1,3-thiazole, 1,3-oxazole, 1,2,3-triazole, 1,2,4-triazole, 1,3,4-thiadiazole, 1,3,4-oxadiazole, 1,2,3,4-tetrazole, quinoline, isoquinoline, indole, 1,3-benzoxazole, 1,3-benzothiazole, benzimidazole, [1,3]oxazolo[4,5-b]pyridine, [1,3]thiazolo[4,5-b]pyridine, [1,2,3,4]tetrazolo[1,5-b]pyridazine and purine, and wherein said Het group can be substituted with one to three substituents selected from C_1-C_4 alkyl, phenyl, pyridyl,

benzyl, C_{1-4} alkoxy, methylthio, fluoro, chloro, nitro, cyano, hydroxy, oxo, amino, methylamino, dimethylamino, 2-dimethylaminoethyl, acetamido and acetyl; and

(d) 2,5-dioxo-1-imidazolidinyl or 2,4-dioxo-1-imidazolidinyl, either of which is optionally substituted at the carbon atom by one or two methyl, linear or branched C_2-C_4 alkyl, phenyl, benzyl or hydroxymethyl groups, and at the nitrogen atom with C_1-C_4 linear or branched alkyl;

or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 which is an isomer having the configuration depicted in formula (I'):



(I')

wherein X, R_1 and R_2 are as defined in claim 1.

3. A compound according to claim 1 which is selected from:

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic acid;

(2*S*)-3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(phenylsulfanyl)methyl]-propanamide;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(4 hydroxyphenyl)sulfanyl]methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[[(4-hydroxyphenyl)sulfanyl]-

methyl]propanamide;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-(phenoxymethyl)propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-(phenoxymethyl)propanamide;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(2-pyridinylsulfanyl)methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(2-pyridinylsulfanyl)methyl]-propanamide;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(2-pyridinylmethyl)sulfanyl]methyl]-propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[[(2-pyridinylmethyl)sulfanyl]-methyl]propanamide;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]-methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]methyl]propanamide;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(5-amino-1,3,4-thiadiazol-2-yl)-sulfanyl]-methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(1-methyl-1H-imidazol-2-yl)sulfanyl]-methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(2-pyrimidinylsulfanyl)methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(1-methyl-1H-tetrazol-5-yl)sulfanyl]methyl]-

propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(1-benzyl-1H-tetrazol-5-yl)sulfanyl]methyl]-

propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(1H-benzimidazol-2-ylsulfanyl)methyl]-propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(1,3-thiazol-2-ylsulfanyl)methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(2-methyl-2H-1,2,3-triazol-4-yl)sulfanyl]-methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(5-phenyl-1,3,4-oxadiazol-2-yl)sulfanyl]-methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[[1-(3-pyridinyl)-1H-imidazol-2-yl]sulfanyl]-methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(4-methyl-1,3-oxazol-2-yl)sulfanyl]methyl]-propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[([1,3]oxazolo[4,5-b]pyrimidin-2-yl-sulfanyl)-methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[([1,2,3,4]tetrazolo[1,5-b]pyridazin-6-yl-sulfanyl)methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(2,6-dimethyl-4-pyrimidinyl)sulfanyl]-methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(4,6-dimethyl-2-pyrimidinyl)sulfanyl]-methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(4-hydroxy-6-methyl-2-pyrimidinyl)-sulfanyl]methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(4,6-dihydroxy-2-pyrimidinyl)sulfanyl]-methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(9H-purin-6-ylsulfanyl)methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-(3-fluorophenoxymethyl)propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(2-acetylaminophenoxy)methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(4-acetylaminophenoxy)methyl]propanoic acid;

3-([1,1'-Biphenyl]-4-ylsulfonyl)-2-[(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)methyl]-

propanoic acid;
3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)-
methyl]propanoic acid;
(2*R*)-3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)methyl]propanoic acid;
3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)methyl]propanamide;
3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(4,4-dimethyl-2,5-dioxo-1-imidazolidinyl)-methyl]propanoic acid;
3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(4,4-dimethyl-2,5-dioxo-1-imidazolidinyl)methyl]propanamide;
3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(2,5-dioxo-1-imidazolidinyl)methyl]propanoic
acid;
3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(2,5-dioxo-1-imidazolidinyl)-methyl]propanamide;
3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(3-methyl-2,5-dioxo-1-imidazolidinyl)-methyl]propanoic acid;
3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(3-ethyl-2,5-dioxo-1-imidazolidinyl)methyl]-
propanoic acid;
3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(3-butyl-2,5-dioxo-1-imidazolidinyl)methyl]-
propanoic acid;
3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(3-butyl-2,5-dioxo-1-imidazolidinyl)methyl]propanamide;
3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(3-butyl-2,4-dioxo-1-imidazolidinyl)methyl]-
propanoic acid;
3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(3-butyl-2,4-dioxo-1-

imidazolidinyl)methyl]propanamide;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(5-isopropyl-2,4-dioxo-1-imidazolidinyl)-methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(5-hydroxymethyl-2,4-dioxo-1-imidazolidinyl)methyl]propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(5-hydroxymethyl-3-methyl-2,4-dioxo-1-imidazolidinyl)methyl]propanoic acid;

3-[(4'-Fluoro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic acid;

3-[(4'-Fluoro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(phenylsulfanyl)methyl]-propanamide;

3-[(4'-Fluoro[1,1'-biphenyl]-4-yl)sulfonyl]-2-(phenoxymethyl)propanoic acid;

3-[(4'-Fluoro[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-(phenoxymethyl)propanamide;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic acid;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(phenylsulfanyl)methyl]-propanamide;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-(phenoxymethyl)propanoic acid;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-(phenoxymethyl)propanamide;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-(3-fluorophenoxymethyl)propanoic acid;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(2-acetylamino)phenoxymethyl]propanoic acid;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(2-pyridinylsulfanyl)methyl]propanoic acid;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[(2-pyridinylmethyl)sulfanyl]methyl]-propanoic acid;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(3-butyl-2,5-dioxo-1-imidazolidinyl)methyl]-propanoic acid;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-N-hydroxy-2-[(3-butyl-2,5-dioxo-1-imidazolidinyl)methyl]propanamide;

3-[(4'-Cyano[1,1'-biphenyl]-4-yl)sulfonyl]-2-[(5-hydroxymethyl-2,4-dioxo-1-imidazolidinyl)methyl]propanoic acid;

3-[[4-(Benzoylamino)phenyl]sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic acid;

3-[[4-(Benzoylamino)phenyl]sulfonyl]-N-hydroxy-2-[(phenylsulfanyl)methyl]-propanamide;

3-[[4-(Benzoylamino)phenyl]sulfonyl]-2-[[(2-pyridinylmethyl)sulfanyl]methyl]propanoic acid;

3-[[4-(Benzoylamino)phenyl]sulfonyl]-2-[(2-thienylsulfanyl)methyl]propanoic acid;

3-[[4-(Benzoylamino)phenyl]sulfonyl]-2-(phenoxymethyl)propanoic acid;

3-[[4-[(4-Methylbenzoyl)amino]phenyl]sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic acid;

3-[[4-[(4-Methylbenzoyl)amino]phenyl]sulfonyl]-N-hydroxy-2-[(phenylsulfanyl)methyl]-propanamide;

3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic acid;

3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-N-hydroxy-2-[(phenylsulfanyl)methyl]-propanamide;

3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-2-(phenoxymethyl)propanoic acid;

3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-N-hydroxy-2-(phenoxymethyl)-propanamide;

3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-2-(3-fluorophenoxymethyl)propanoic acid;

3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-2-[[(2-pyridinylmethyl)sulfanyl]methyl]-propanoic acid;

3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]-2-[[(1-methyl-1H-tetrazol-5-yl)sulfanyl]-methyl]propanoic acid;

3-[[4-[(4-Chlorobenzoyl)amino]phenyl]sulfonyl]- 2-[(5-hydroxymethyl-2,4-dioxo-1-imidazolidinyl)methyl]propanoic acid;

3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-2-[(phenylsulfanyl)methyl]propanoic acid;

3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-N-hydroxy-2-[(phenylsulfanyl)methyl]-propanamide;

3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-2-[[(1-methyl-1H-tetrazol-5-yl)sulfanyl]-methyl]propanoic acid;

3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-2-(phenoxymethyl)propanoic acid;

3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-N-hydroxy-2-(phenoxymethyl)-propanamide;

3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-2-(3-fluorophenoxymethyl)propanoic acid;

3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-N-hydroxy-2-(3-fluorophenoxymethyl)-propanamide;

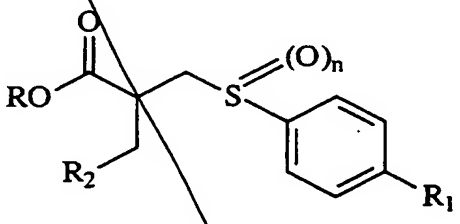
3-[[4-[(4-Cyanobenzoyl)amino]phenyl]sulfonyl]-2-[(2-acetylamino)phenoxymethyl]-propanoic acid;

3-[[4-(4-Propylbenzoylamino)phenyl]sulfonyl]-2-[[(1-methyl-1H-tetrazol-5-yl)sulfanyl]-methyl]propanoic acid; and

3-[[4-[(4-Methoxybenzoyl)amino]phenyl]sulfonyl]-2-(phenoxymethyl)propanoic acid;

3-[(4'-Chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-[[2-(hydroxymethyl)phenoxy]methyl]-propanoic acid; and the pharmaceutically acceptable salts thereof.

4. A process for producing a compound as defined in claim 1, starting from a compound of formula 4:



(4)

wherein R is H or the residue of a carboxylic acid ester, R_1 and R_2 are as defined in claim 1 and n is 0 or 2, which process comprises:

(a) hydrolysing a said compound of formula 4 in which R is the residue of a carboxylic and ester to give a compound of formula (I) in which X is HO-; or

(b) hydrolysing and oxidising, in either order, a said compound of formula 4 in which n is 0 and R is the residue of a carboxylic acid ester, to give a compound of formula (I) in which X is HO-; or

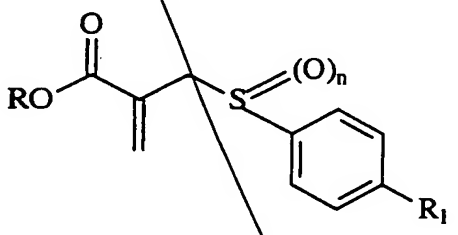
(c) activating a said compound of formula 4 wherein R is H and n is 2 to form an activated carboxy group, coupling the activated carboxy group with hydroxylamine or an O-protected derivative thereof and, if necessary, deprotecting the hydroxamic group to give a compound of formula (I) wherein X is –NHOH; or

(d) submitting a said compound of formula 4 wherein R is H and n is zero to a sequence of reactions comprising oxidation at the sulphur atom, activation of the carboxy group, condensation of the activated carboxy group with hydroxylamine or an O-protected derivative thereof and, if necessary, deprotection of the hydroxamic group to form a compound of formula (I) wherein X is –NHOH, the oxidation step being conducted either before the activation step or after the condensation step; and/or

(e) if desired, converting a resulting compound of formula (I) into another compound of formula (I); and/or converting a free compound into a pharmaceutically acceptable salt thereof; and/or converting a salt into a free compound.

5. A process according to claim 4 wherein the compound of formula 4 is obtained by

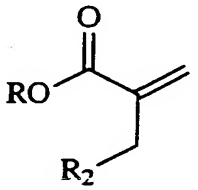
(a) subjecting a compound of formula 2:



(2)

wherein R, R_1 and n are as defined in claim 4, to conjugate addition by treatment with a compound of formula R_2H wherein R_2 is as defined in claim 1; or

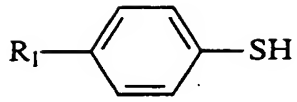
(b) treating a compound of formula 3:



(3)

wherein R and R_2 are as defined in claim 4, with a thiol of formula:

Sub A2



to obtain a compound of formula 4 in which n is zero.

6. A pharmaceutical composition which comprises a pharmaceutically acceptable carrier or diluent and, as an active principle, a compound as defined in any one of claims 1 to 4.

7. A compound as defined in any one of claims 1 to 4, for use in a method of treatment of the human or animal body by therapy.

8. A compound as claimed in claim 7 for use in the treatment or prophylaxis of a disease in a mammal mediated by a matrix metalloproteinase.

9. A compound as claimed in claim 8 wherein the matrix metalloproteinase is a gelatinase (MMP-2), the membrane-type MMP involved in gelatinase activation (MMP-14), a stromelysin (MMP-3 or MMP-10), collagenase (MMP-13) or neutrophyl collagenase (MMP-8).

10. A compound as claimed in any one of claims 7 to 9 for use in the treatment or phophylaxis of tumour growth or metastasis, rheumatoid arthritis, osteoarthritis, ophthalmic disease, cardiovascular disease, periodontal disease, multiple sclerosis or Alzheimer's disease.

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